REMARKS

Claims 39, 40, 42, and 45-48 were pending in the present application. Applicant has added new claims 49-50, which are supported in the specification and do not include new matter. For example, new claims 49-50 are supported in the specification at page 40, lines 28-29 and in the claims as originally filed. Thus, claims 30, 40, 42 and 45-50 are pending.

Applicant gratefully acknowledges the withdrawal of previous 35 U.S.C. § 112, first paragraph rejections of claims 31 and 39-47 (Office Action, page 2). Applicant also gratefully acknowledges the withdrawal of 35 U.S.C. § 112, second paragraph rejections labeled a) and b) at page 7 of the previous Office Action dated 09/18/2002 (Office Action dated 07/08/03, page 3). Furthermore, Applicant gratefully acknowledges the Examiner's indication that dependent claim 48 is allowable if rewritten in independent form. Applicant addresses each of the remaining objections and rejections, and respectfully request reconsideration in view of the following discussion.

Objections Relating to Formal Matters

The Examiner made various objections relating to formal matters. With regard to the Examiner's request for a copy of the references cited in the Information Disclosure Statement filed October 17, 2001, Applicant hereby submits the references, attached as Exhibit 1.

With regard to the defective declaration, Applicant submits a properly executed substitute declaration by Dominique Schols, attached as Exhibit 2. With regard to a claim for priority, the specification has been amended to include a cross-reference to prior-filed applications. The specification has also been amended to correct typographical errors. Accordingly, Applicant requests that these objections relating to formal matters be withdrawn.

The Rejections Under 35 U.S.C. § 112, Second Paragraph

As previously indicated, Applicant gratefully acknowledges the withdrawal of 35 U.S.C. § 112, second paragraph rejections labeled a) and b) from the previous Office Action dated 09/18/2002. However, the Examiner maintained the rejection labeled c) from the previous Office Action. As a preliminary matter, Applicant notes that the rejection labeled c) from the previous office action was a 35 U.S.C. § 112, second paragraph rejection. Because the Examiner had withdrawn 35 U.S.C. § 112, first paragraph rejections of claims 31 and 39-47 and the rejection labeled c) is a 35 U.S.C. § 112, second paragraph rejection, Applicant addresses this rejection as a 35 U.S.C. § 112, second paragraph rejection.

Claim 39 was previously rejected under 35 U.S.C. § 112 second paragraph as allegedly vague and indefinite for failing to set forth "any steps involved in determining which are the diseases capable of being mediated by a chemokine receptor." (See Office Action dated 09/18/02, page 7). Applicant must respectfully disagree. Contrary to the Examiner's assertions, claim 39 clearly points out the subject matter which Applicant regards as the invention.

In particular, claim 39 relates to a method for treating or ameliorating a CXCR4 mediated disease by administering an effective amount of AMD 3100. Claim 39 does not recite steps for determining which diseases are mediated by chemokine receptors because claim 39 does not relate to methods for determining which diseases are mediated by chemokine receptors. Furthermore, Applicant has discovered that AMD 3100 modulate the activity of the chemokine receptor CXCR4, and thus provides a readymade treatment for any diseases later found to be mediated by CXCR4.

Applicants appreciate the careful analysis made by the Office regarding the difficulties in evaluating drug efficacy and the necessity of optimizing the treatment regime. The conclusion drawn from of this analysis, however, is that the metes and bounds of the claim are putatively uncertain because individual responses may differ or incorrect dosages may apply. However, claim 39 will be infringed when AMD 3100 is administered to a subject in need of treatment or amelioration of a CXCR4 mediated disorder.

With respect to paragraph (A), it is not required that the patient actually respond for the claim to be infringed. As long as the patient has been diagnosed with the relevant condition, and

as long as a generally effective dose has been determined for that condition, the claims would have been infringed. With respect to paragraph (B), it is recognized that for each composition a variety of methods of administration may be employed. It is routine to optimize such administration.

With respect to paragraph (C), it is also recognized that not all drugs successful *in vitro* are successful in the clinic. However, success in the clinic is not a criterion for patentability. This was made clear in *In re Brana*, 34 USPQ2d 1437 (Fed. Cir. 1995), where the court specifically stated that efficacy in clinical settings is the province of the FDA, not the patent office.

With respect to paragraph (D), again, claim 39 will be infringed when AMD 3100 is administered to a subject in need of treatment or amelioration of a CXCR4 mediated disorder. Similar comments apply to paragraph (E), and again, the Office is reminded that infringement occurs whether or not an individual patient responds to the treatment. Because claim 39 clearly points out the subject matter which Applicant regards as the invention, Applicant respectfully request that this rejection be withdrawn.

The Rejection Under 35 U.S.C. § 112, First Paragraph

As previously indicated, Applicant gratefully acknowledges the withdrawal of previous 35 U.S.C. § 112, first paragraph rejections of claims 31 and 39-47 (Office Action, page 2). However, the Examiner issued a new ground of rejection, which Applicant addresses below.

Claims 42, 45 and 47 were rejected under 35 U.S.C. § 112 first paragraph, as allegedly containing subject mater which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention. The Examiner alleged that the specification lacked a written description of leukemia, central nervous system developmental disease and cardiogenesis developmental disease. Applicant must respectfully disagree.

Contrary to the Examiner's assertions, the specification contains more than adequate written description for the disorders central nervous system developmental disease and

cardiogenesis developmental disease. (See e.g., specification at page 40, line 31, and at page 41, lines 27-28). Furthermore, to expedite prosecution without acquiescing to the Examiner's arguments, Applicant has amended claim 42 to recite only lymphoma. Accordingly, this rejection is moot and Applicant respectfully requests that this rejection be withdrawn.

The Rejections Under 35 U.S.C. § 102

Claim 39 was previously rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Schols *et al., J. Exp. Med.* 186: 1383-1388 (1997). In view of the enclosed executed *Katz* declaration, attached at Exhibit 3, this publication is discounted as prior art since its publication date was not prior to Applicant's priority date of July 8, 1998. Accordingly, Applicant requests that this rejection be withdrawn. The Examiner also issued new grounds of rejections, which the Applicant addresses below.

Claim 40 is rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Winchester *et al.* (U.S. 2002/0039993). Applicant must respectfully disagree. Contrary to the Examiner's assertions, Winchester *et al.* is not prior art. Specifically, the 102(e) date of the Winchester publication, July 31, 1998, is subsequent to the priority date of the present application, July 8, 1998. Thus, Applicant respectfully request that this rejection be withdrawn.

Furthermore, claim 39 is rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Luster *et al.* (U.S. 2002/0033841). Applicant must respectfully disagree. In view of the Declaration of Dominique Schols Pursuant to 37 C.F.R. § 1.131 (Schols' 1.131 Decl.), attached at Exhibit 4, the Luster publication is discounted as prior art since its filing date, June 19, 1998, was not prior to Applicant's invention. Specifically, Applicant has discovered that AMD 3100 interacts with the chemokine receptor CXCR4 prior to June 19, 1998, as evidenced by Applicant's publications, Schols, D. *et al., J. Exp. Med.* 186: 1383-1388 (1997) and Schols, D. *et al., Antiviral Res.* 35: 147-156 (1997) (See Schols' 1:131 Decl., ¶ 3). Thus, Applicant respectfully request that this rejection be withdrawn.

The Rejections Under 35 U.S.C. § 103(a)

Claims 39, 46 and 47 were rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable under Luster *et al.* (U.S. 2001/0033841) in view of Tachibana *et al.*, *Nature* 393: 591-594. Applicant must respectfully disagree. As previously indicated, the Schols' 1.131 Declaration discounts the Luster publication as prior art. Thus, the only relevant prior art is Tachibana *et al.*

Contrary to the Examiner's assertions, claims 39, 46 and 47 are nonobvious under Tachibana *et al.* The Tachibana reference teaches the role of CXCR4 in the vascularization of the gastrointestinal tract. However, Tachibana is silent with regard to AMD 3100. Because Tachibana simply fails to teach AMD 3100, let alone methods for using AMD 3100 for treating or ameliorating a CXCR4 receptor mediated disorder, claims 39, 46 and 47 are nonobvious. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Furthermore, claims 39, 40 and 45 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable under Luster *et al.* (U.S. 2001/0033841) in view of Zou *et al.*, *Nature* 393: 595-599. As previously indicated, the Schols' 1.131 Declaration discounts the Luster publication as prior art. Thus, the only relevant prior art is Zou *et al.*

Contrary to the Examiner's assertions, claims 39, 40 and 45 are nonobvious under Zou *et al.* The Zou reference teaches the function of CXCR4 in haematopoiesis and in cerebellar development. However, Zou is silent with regard to AMD 3100. Because Zou simply fails to teach AMD 3100, let alone methods for using AMD 3100 for treating or ameliorating a CXCR4 receptor mediated disorder, claims 39, 40 and 45 are nonobvious. Accordingly, Applicants respectfully request that this rejection be withdrawn.

New claims 49-50

New claims 49-50 are dependent claims relating to methods for treating or ameliorating CXCR4 mediated disorders, namely a disorder comprising basal leukocyte trafficking and a disorder comprising extravasation and tissue infiltration of leukocytes in response to inciting antigens. As previously indicated, these claims are supported in the specification and do not include new matter. Furthermore, these claims are neither anticipated nor obvious under any

prior art the Examiner has cited for the reasons stated above. These claims are also clear in scope and enabled for the reasons stated above. Thus, these claims are allowable.

Duty of Disclosure

Finally, to comply with the duty of disclosure, Applicant submits a second *Katz* declaration, attached as Exhibit 5, discounting Donzella *et al.*, *Nature Medicine* 4: 72-77 (January 1998) as a prior art reference. The Donzella reference was listed on the Information Disclosure Statement submitted on October 17, 2001. However, the Examiner has not cited this reference as prior art. Because the Donzella reference describes Applicant's own work, the reference is not prior art.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding claim rejections and pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 391442001122.

Respectfully submitted,

Dated: December 8, 2003 By: _____

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